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STUDIES OF THE EFFECTS OF GRAVITATIONAL AND INERTIAL FORCES ON CARDIOVASCULAR AND RESPIRATORY DYNAMICS

The major portion of this report consists of status reports on three investigative projects which have received support from this grant.

Section I is a continuation of the assessment reported in the April 1, 1970 report concerning the reproducibility and accuracy of the biplane roentgen videometry system which has been developed for dynamic (60 per second) measurements of the shape and volume of the left ventricle in intact animals and man.

Section II is a progress report on the current status of the continuing investigations of the effects of the magnitude and duration of the gravitational-inertial force environment on intrathoracic pressure relationships and the consequent alterations in the spatial distribution of pulmonary blood flow.

Section III is a progress report on a study of the effects of water immersion and breathing liquid fluorocarbon on the cardiopulmonary effects of acceleration.

I. ROENTGEN BIPLANE VIDEOMETRY

Study of the effects of gravitational and inertial forces on cardiovascular and respiratory dynamics in large mammals, including man, requires the development of quantitative methods for measuring cardiovascular and respiratory function which can be used without thoracotomy and without appreciable morbidity to the subjects under study.

The techniques of roentgen videometry and videodensitometry, which have been developed in this laboratory, have this capability. This system has been fully described in previous reports (October 1968, April and October 1969, and April 1970) and only a brief description follows.

The roentgen biplane videometry system developed at this institution became fully operational upon the delivery of the Ampex Model DR 10 video disc on August 25, 1970. The only feature of the system that is not operational as yet is the 16-channel data recording capacity which will soon be added to the present videotape and disc recording system. Presently, only two data tracks are available on the videotape, limiting the analog data which can be recorded synchronously on the same videotape with the biplane angiogram to left ventricular pressure and the electrocardiogram. The ECG trace is superimposed on the recording of the rate and volume of injection of the contrast medium. The details of the system have been described in previous reports, and only a brief description follows.

Biplane roentgenographic images of the left ventricular angiograms are recorded on videotape simultaneously with left ventricular pressure, ECG, and the rate and volume of injection of radiopaque indicator (69% renovist) into the left ventricle. The operator, on an interactive basis, uses the flying-spot scanner and the video quantizer assembly to process the video signal so that, in his judgement, the video display of the border recognition points generated by the quantizer system circumscribes and coincides perfectly with the borders of the biplane image of the opacified left ventricular cavity. Any nonangiographic radiopacities which may interfere with border recognition, such as the diaphragmatic border of the liver, can be preferentially shaded out by the operator with the use of the flying-spot scanner system. Undyed blood entering the left ventricle via the mitral valve during diastole produces a less radiopaque area or hole in the roentgen image of the ventricular cavity just downstream to the mitral valve. This problem has been overcome by the operator being able to preferentially darken the affected area within the confines of the ventricular silhouette, using the flying-spot scanner system. Small regions of erroneous border recognition can also be removed at a later stage by digitally interpolating across the "defect" in the cardiac border.

The values from four 10-bit counters represent the position in space of each of the four border recognition points on each of the 60 to 80 horizontal video lines which generate the two images of the ventricle. These are then transferred to the CDC 3300 digital computer in real time. This requires a data transfer rate of approximately 63,000 data points per second.

After a complete video field has been scanned, the data for that field is transferred to a digital magnetic tape. Real-time scanning of one to three heart cycles lasting several seconds can be achieved by using only a standard 2200 word computer program written in basic assembly language. Moreover, the time-sharing capability of the 3300 computer Medlab monitor system is interrupted for only the two to three seconds required to obtain all the data from these heart beats. On completion of this rapid data transfer procedure, the computer returns to its time-sharing mode of operation, taking up the "interrupted" programs at the point where they were interrupted at the start of the scan.

When the data acquisition from the video disc is completed, the digital tape is read and the data analyzed and displayed on a storage oscilloscope at a peripheral computer station juxtaposed to the videotape-videodisc data processing assembly. The displayed information may be in the form of the calculated volume of the ventricle and the simultaneous ventricular pressure for each of the one to three-hundred sequential video fields analyzed. Figure 1 illustrates the analysis of one-hundred video fields recorded during the rotation of a cast of the left ventricle about its longitudinal axis through 180 degrees in about one second during which sixty fields were recorded while the subsequent forty fields were recorded when the position of the cast was stationary. The one-hundred computed volumes of the ventricular cast are plotted against its angular position during the period of rotation and against time during the period it was stationary. The right panel is the same as the left panel except that the rotated object is a radiopaque sphere. Individual video fields may be selected by the operator from the sequence of fields and the "raw" data for that field displayed in the form of the biplane silhouettes of the object under study (e.g., the left ventricular cavity, as shown in Figure 2). On the basis of these computer generated oscilloscopic displays, a rapid assessment as to the success of the data transfer, as well as the identification of a sequence of video fields in which the border recognition may not be optimal, can be readily made by the operator. Detailed analysis and display of the data can be subsequently performed at leisure using the more powerful non-time sharing mode of operation of the MSOS monitor system of the CDC 3300 computer.

The accuracy and reproducibility of the data has been assessed. This system utilizes the experience and pattern recognition ability of the operator to judge whether or not the borders of the ventricular silhouettes which have been detected electronically by the videometry system are accurate. This capability prevents the possibility of bizarre borders being analyzed, thereby removing the possibility of grossly incorrect data being collected. This essential feature, however, introduces significant variation in results since the operator interactive adjustment of the system to obtain what is judged to be the closest possible coincidence of the border recognition points with the actual border, introduces variations of about 1.5% in the computed volume of an average size left ventricular chamber. This variation in volume corresponds to an error of less than 0.4 mm in the measurement of the diameters of the real object. The variability in the calculated volumes due to uncontrolled variations in the video signal and other electronic causes is about 0.6% in ventricles of about 50 ml volume, and increases significantly for small ventricular chambers, particularly at the end-systolic phase of the cardiac cycle. The accuracy of the calculated volume of an ellipsoid-like object from the biplane data was tested with radiopaque filled balloons. Biplane, 60-per-second roentgen images of a balloon were recorded on videotape during injections of a known volume of dye (69% renovist) into the balloon. This videotape recording was analyzed in real time for the one-to-three second injection period of the dye during replay of the videotape recording. Figure 3 is a computer generated plot of the computed values of balloon volume against the number of 60-per-second biplane videofields from which the measurements of volume were made. The calculated volume of the balloon was correct to within 0.2 ml for balloons in the 30 to 40 ml range.

The biplane videoangiograms view the ventricle in two orthogonal planes only and the shape of the ventricle, when viewed at angles different from these two views, is not accurately known for a ventricle viewed in the intact chest. Presently, the the ventricle is assumed to be elliptical in circumference at any one plane transecting the cavity. It is obvious that the irregularities of the ventricular trabeculations and papillary muscles make this assessment false, although it appears to be reasonable as a first approximation. If the correct "model" for the shape of the left ventricular cavity were known, then the true volume of the cavity could be calculated for any known angular aspect of the ventricular cavity viewed by the biplane x-ray field. Three assumed shapes ("models") of the left ventricular cavity have been used to calculate the volume of casts of the left ventricular cavity.

Silastic casts of the canine left ventricle (supplied by Dr. Harold Sandler) were impaled on thin rods along the longitudinal axis of the casts, as shown in Figure 4. These casts were mounted at an adjustable angle from the plane of the x-ray beam of the biplane video system and centered at the intersection of these beams. The rotational position of the cast about its longitudinal axis was monitored by a circular potentiometer. Biplane roentgen images of the cast and its angular position about its longitudinal axis were recorded on videotape as the casts were rotated 360 degrees in two seconds.* This procedure was repeated at different angles of the axis and for casts made at different phases of the cardiac cycle. Three sets of values for ventricular volumes were calculated based on three assumed shapes of this chamber as follows: It was assumed that the shape of each of the 60-80 cross sections delineated by each of the 60-80 horizontal video lines constituting the biplane video images was truly elliptical and that the orthogonal diameters measured from each of these horizontal lines were the actual major and minor diameters of each of these assumed elliptical discs. Based on this assumption:

1) $$\Delta V_n = \pi * K * ((B_n - A_n) /2) * (D_n - C_n) /2))$$

where ΔV_n is the volume of the disc
K is the scaling factor
A_n, B_n, C_n, D_n are the coordinates of the 4 borders at level n

$$\text{Total Volume} = \sum_{n=1}^{N-1} \Delta V_n$$

* These casts were transradiated by 60 kv x-rays so that the radiopacity of the casts closely matched that of the left ventricular cavity outlined graphically in the intact thorax.

It was assumed that the ventricular cavity is spheroidal in shape and that major and minor diameters of each silhouette in the biplane images were the true major and minor axes of this spheroid. Based on this assumption:

2) Total Volume = $\pi * L * D_a * D_b/6$

where D_a and D_b are the two minor axes calculated in the relationship
$D = 4A/\pi * L$
A is the area of each respective silhouette
L is the longest diameter of the two silhouettes

It was assumed that the ventricular cavity was a prolate spheroid in shape. Based on this assumption, the volume of the cavity was calculated from each monoplane image:

3) Total Volume = $\pi * L * D_a * D_b/6$

the symbols are the same as for Method 2, but D_a is obtained from each monoplane silhouette directly, and D_b from the relationship
$D_b = 4A/\pi * L$

Figure 5 shows a much expanded plot of the calculated volume values obtained during rotation of the cast using the multiple elliptical disc method and Simpson's rule for integration of their volumes. The calculated values were always greater than the true volume of the cast. It is of interest to note the 90-degree periodicity in the variation of these calculated values in relation to the angular position of the cast. This results from observation in two fixed orthogonal planes of a rotating object which has one dominant diameter, such as occurs in a cross or an ellipse. Analysis of this periodicity of calculated volume during rotation of the cast provides information as to the effective shape of the rotating object (i.e., the roentgenographic image). The simultaneous volume values calculated on the basis of all three assumptions are plotted in Figure 6. Note that the monoplane data has a 180-degree periodicity, and that values obtained by summing the 60 to 80 assumed elliptically shaped cross sections of the cast (Method 1) give values closest to the true volume at all angular positions. Values based on the ellipsoid assumption (Method 2) using four axes measured from the orthogonal silhouettes resulted in a greater overestimate than Method 1, whereas the values based on monoplane views (Method 3) generally gave the greatest overestimate.

Figure 7 shows the correlation of the calculated volume for this ventricular cast using the elliptical disc and ellipsoid assumptions, respectively. There is a 1:1 relationship with a 2.4 ml offset between the two determinations which represents a 5% difference in volume between the two methods. Figure 8 shows the correlation between the multiple elliptical disc and monoplane methods. The correlation is poor when taken over an entire 180-degree range, but over restricted ranges of angular position, the correlation is quite good.

These data were obtained when the cast was oriented so that its long axis was at right angles to the plane of the x-ray beams. When the long axis of the cast is not orthogonal to thisplane, the relationship of the volumes calculated by the three methods during rotation of the cast alters so that on the average these values overestimate the actual volume by a greater degree than when the axis is oriented at right angles to the plane of the x-ray beams. The variation is also greater to the extent that the minimum calculated volume by the monoplane method may actually be less than the true volume. When these observations were carried out using casts obtained at different phases of the cardiac cycle, similar patterns in the variation of the calculated volumes were obtained. In all cases, however, the values based on biplane measurements showed 30 to 50% less variation with rotation than the values obtained by the monoplane method. Values based on the ellipsoid model differed from the elliptical disc model by a fixed volume offset, and the two sets of values exhibited a nearly 1:1 relationship. On the average, the calculated volume values for the four different casts (made at different phases of the cardiac cycle) obtained by the ellipsoid method and the monoplane method, respectively, were 3 and 7%, respectively, larger than the values obtained by the multiple elliptical disc method.

These methods for calculation of left ventricular volume have also been used to determine the volumes of the left ventricular chamber visualized in the intact thorax of anesthetized dogs by videoangiography. Left posterior and anterior oblique projections of the left ventricle were recorded during injections of 69% renovist, as described above. Figure 9 shows the calculated left ventricular volumes and pressures calculated 60 times per second during one heart cycle in a dog with chronic heart block, a slow idioventricular rhythm and consequent cardiac decompensation. Note that small (1-2 ml) changes in calculated volume of the ventricular cavity were obtained during the isovolumic contraction and relaxation phases. These are probably due to changes in the shape of the ventricular cavity without a volume change which would produce changes in the length relationships of the two diameters and hence in the calculated volumes of the "discs" and also to the random variations in the calculated volume values due to the inevitable small errors in recognition of the margins of the multiple discs comprising this cavity. There was no angiographic evidence of mitral reflux in this angiogram. Figure 10 shows simultaneous volume values by the three methods every one-sixtieth of a second during the same heart cycle. It is clear that despite the fixed volume offset between the three values at any one point in time, the major features of the volume change with time are evident in all sets of values. The intercorrelations between the three sets of values is shown in Figures 11-12.

It is clear from these preliminary studies that greater knowledge about the shape of the left ventricle, as obtained by biplane angiography, is needed before realistic correlations between such parameters as stroke volume, ECG, and left ventricular pressure and dynamic changes in left ventricular geometry and associated length and tension changes in the myocardium can be obtained and interpreted in relation to cardiac function. The volume of the left ventricular cavity and the curvature of the myocardial wall containing this cavity are a function of the shape of the left ventricular cavity. Both volume and curvature and the associated myocardial length and tension relationships are of particular interest in their relationship to ventricular function. However, the relationship of the shape and volume of radiographic images of the left ventricular cavity to the true physical shape and volume of the cavity is complex. The degree of opacification of the cavity by the blood-contrast medium mixture is variable, particularly at the endocardial surfaces resulting in variable contrast at the borders of the cavity silhouettes. Consequently, understanding of the shape of left ventricular cavity in the intact animal requires knowledge of this shape and how the visualization of this shape is affected by the particular orthogonal projections and body position used in angiography and the angiographic procedure per se. The effectively greater resolution of angiographic analysis using the electronically assisted videometry system, as compared to "hand" analysis of the same angiograms is possible because of the capacity for real-time computer analysis reduces analysis times to practical dimensions while still maintaining the maximal resolution in time and space of the full scope of the videoangiographic images obtained during each injection of contrast medium. Since the results reported in this and prior progress reports have demonstrated that the values for the volume of the left ventricular cavity obtained 60 times per second and using the biplane roentgen videometry technique and the assumption of an elliptical shape for multiple cross sections of this cavity are reasonably accurate, application of this method to studies of cardiovascular physiology are being initiated. A series of experiments has been started to compare the videometric analysis of angiocardiograms with more conventional means of measuring the cardiac output, such as conventional dye-dilution technique and beat-to-beat measurement of stroke volume obtained by chronically implanted aortic electromagnetic flowmeter and analysis of aortic pressure pulses. Other related experiments include the determination of the atrial contribution to ventricular stroke volume under conditions of different atrial-ventricular stimulus delay in the electronically paced complete heart block dogs. Preliminary data indicate that there is good correlation between the simultaneous determinations of stroke volume obtained by these three independent methods (Figs. 13-15). These data indicate that the videometry system can be used as an autonomous technique in the investigation of ventricular function where beat-to-beat data is of interest and not accessible by conventional means in animals or man studied without thoracotomy. The effect of autonomic tone, altered either by nerve stimulation or denervation as well as by humoral means, on the ventricular volumes and shape can be studied. It appears that ventricular shape will become an increasingly important parameter in the characterization of left ventricular function.

Preliminary studies of the effects of the shape of the left ventricular cavity on the values for its volume calculated by biplane videometry suggest that some generalities can be made. The calculated volume of cross sections of the left ventricular cavity at each of the up to 80 points along its longitudinal axis fell roughly into three regions of behaviour when the casts of the cavity were rotated about their long axes and the cross sections were assumed to be elliptical in shape (Figures 16-17). The calculated volumes of the cross sections in the basal third of the cavity of casts made at end-diastole and end-systole vary little during a full 360-degree rotation of the cast. This suggests that the shapes of these cross sections, as determined by this technique, are close to circular in this region of the cavity.

The calculated volumes of the cross sections making up the middle third of the cavity in which region the invaginations of the papillary muscles occur show the most variation during rotation of the cast. This indicates that the shape of the cross sections in this region is not circular. The cross sections of the apical third of the cast made at end-diastole show little variation in calculated cross-section volumes of the apical region. It is impossible to say from these data whether this difference between diastole and systole is due to partial obliteration of the cavity in the apical region of the ventricle during systole with consequent irregularities in its shape, or if there is a generalized change in shape in the cross sections of the apical region during different phases of the cardiac cycle.

CONCLUSIONS

The biplane roentgen videometry system makes dynamic (60 per second) measurements of the shape and volume of angiographically outlined cardiac chambers along with synchronous ECG, pressure and flow data accessible for digital computer processing and analysis in real time. The two major causes for inaccuracy in the volume measurements are both operator mediated. Firstly, the operator can not reproduce his border recognition judgement to better than 1.5 per cent equivalent in volume, and second, the current assumption that the ventricle has an elliptical cross section produces considerable error in calculated volume values, especially in the case of a small ventricle at the end-systolic phase of the cardiac cycle.

Preliminary studies involving simultaneous measurements of beat to beat stroke volumes by roentgen videometry, and by the more conventional indicator aortic flowmeter and pressure pulse techniques in dogs studied without thoracotomy indicate that the roentgen-video measurements are accurate over a large range of heart rates and stroke volumes.

These studies demonstrate that the roentgen videometry system can be used as an independent quantitative technique for more detailed and sophisticated investigations of ventricular function where beat-to-beat data is of interest and not accessible by conventional means in animals or man studied without thoracotomy.

II. SPATIAL DISTRIBUTION OF PULMONARY BLOOD FLOW: COMPUTER CONTROLLED TECHNIQUES OF MEASUREMENT AND DISPLAY OF THE INFLUENCE OF THE MAGNITUDE AND DURATION OF THE GRAVITATIONAL-INERTIAL FORCE ENVIRONMENT*

The effect of duration, direction, and magnitude of the gravitational-inertial force environment on changes in the spatial distribution of pulmonary blood flow measured with radioactive microspheres was studied in six anesthetized dogs and four chimpanzees while maintianed in the left lateral decubitus posititionby means of form fitting half-body casts.

The distribution of blood flow was determined from the distribution of 35μ or 15μ diameter radioactive microspheres after their injection into the right ventricle and subsequent impaction in the small vessels of the lung. Injection of up to four sets of differentially radioisotopically tagged microspheres were made: during 1G control period in each animal, and at two (dogs) and three (chimpanzees) successive points in time during two-three minute exposures to G_y centripetal acceleration (range:5.6-8.0G) on a 30-foot diameter centrifuge.

The spatial distribution of radioactivity (blood flow) was measured in the dogs by computer controlled scintiscanning at an orthogonal array of points spaced at 0.6 and 0.7 cm in the X and Y axes, respectively, and covering the surface of 1 centimeter thick sections of the lungs. Prior to sectioning, the lungs were inflated, dried in air, and embedded in urethane foam. The counts of radioactivity

* Abstract of a thesis by James Fowler Greenleaf accepted in partial fulfillment of the requirements for a Ph.D. degree in bioengineering.

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over each stored on digital magnetic tape along with the anatomical borders of the individual lobes which were inputed to the digtal computer through a two-dimensional cursor device. The chimpanzees were scintiscanned in vivo.

The volume of lung tissue in each section, lobe, and total lung along with the number of counts at each scan position (blood flow fraction/unit volume of lung tissue) and the total counts (blood flow) in each lobe and lung are determined from these data by digital computer. The resulting data arrays of spatially distributed blood flow per unit of lung volume, flow to the individual lobes and to each lung were displayed on a computer driven oscilloscope as simulated three-dimensional surfaces and as contour maps.

Other physiologic data included continuously recorded oxygen saturation, and intermittently sampled carbon dioxide and oxygen partial pressures and pH of mixed venous (pulmonary arterial) dependent pulmonary venous and mixed arterial blood, intrathoracic, vascular, and respiratory pressures, and biplane roentgenograms of the thorax.

Control studies to determine the efficacy of the microembolization technique in measuring blood flow distribution indicated that injection site (high or low right ventricle), microsphere size (15 or 35μ diameters) and duration of right ventricular injection (1 or 30 seconds) do not appreciably affect the resulting distribution of microspheres. In addition, scintiscans of liver, kidney, and brain indicated that the microspheres did not pass through the microcirculation of the lungs.

Blood flow to the upper regions of the superior lung was decreased uniformly in proportion to the magnitude of the inertial force environment. However, the relative distribution of blood flow to the superior and dependent lungs of dogs and chimpanzees was found to be strongly affected by the occurrence or absence of periodic fast deep breaths which caused an increase in the rate and depth of ventilation. Deep breaths are presumably most effective in increasing the ventilation of the most dependent normally underventilated regiions of the lungs.

This effect may be mediated primarily by the pulmonary hypercapnic vasoconstrictor response. This response is superimposed on and may over-ride the hydrostatic effects which cause the vertical gradients in vascular and pleural pressures due to the gravitational-inertial force environment to which the animal is exposed and which are responsible for the uniformly observed decrease in flow to the most superior regions of the lungs.

III. MODIFICATION OF THE CARDIOPULMONARY EFFECTS OF ACCELERATION BY WATER IMMERSION AND LIQUID BREATHING

The effects of G_y acceleration on cardiovascular and respiratory function in dogs were compared under three conditions: 1) normal respiration in air; 2) totally immersed in a saline-filled chamber providing control of respiratory rate, tidal and residual volumes when breathing air or oxygen, and 3) when respired in the same manner with oxygenated liquid fluorocarbon (FC 80). Pressures in the aorta, pulmonary artery, right and left atria, left pulmonary vein, and right and left pleural spaces were recorded. Oxygen saturations of aortic, pulmonary arterial and left pulmonary vein blood were recorded continuously by cuvette oximetry. The results indicate that: 1) arterial hypoxemia due to dependent pulmonary arteriovenous shunting caused by acceleration is not minimized by water immersion alone; 2) dogs can be respired with liquid fluorocarbon for four hours or longer at 37.5°C without clinical signs of respiratory distress with arterial PCO_2 values controlled between 16 and 40 mm Hg and with arterial blood 100% saturated at breathing rates between four and eight per minute; 3) liquid respiration prevented dependent pulmonary arteriovenous shunting at $+6G_y$; 4) in air-breathing dogs, vertical gradients in pleural pressure were approximately 0.7 cm H_2O/cm vertical distance between pleural catheter tips in contrast to 1.6 cm H_2O/cm vertical distance in fluid-breathing experiments. The specific gravity of the fluorocarbon was 1.7.

The results of such a study, in addition to their academic interest, are of practical importance in relation to the problems of development of dependent atelectasis in immobilized patients and the arterial hypoxemia and occasional instances of damage to pulmonary parenchyma which have been observed at levels of acceleration encountered during the launch and re-entry phases of space flight and the frequent injury to the thoracic contents caused by impact acceleration (vehicular crashes) and blast. If a safe and practical technique for breathing of a liquid with a specific gravity similar to that of blood and tissue can be developed, it appears possible that combination of this technique with immersion in water would allow humans to withstand levels of acceleration of over 50G, such as could be encountered during uncontrolled re-entry of the earth's atmosphere from outer space or during a crash situation.

Liquid breathing also has potential applications in extending man's capability for withstanding sustained or transient extreme changes in environmental pressure such as associated with explosive blasts, sudden decompression, and deep-sea diving. Extravehicular survival by the use of liquid breathing in the extreme depths of the ocean may also be feasibile.

PLANS FOR INVESTIGATIVE PROJECTS DURING THE PERIOD NOVEMBER 1, 1970 - OCTOBER 31, 1971

The work planned for the fourth year of the investigative program supported by this grant will be in close accord with the five-year projection contained in the original grant request submitted August 21, 1967, and outlined in the April 1970 progress report for the current grant period.

A. Development of biplane roentgen videometry for study of cardiovascular function of man and intact animals during exposure to changes in the gravitational-inertial force environment and other forms of cardio-respiratory stress.

1. The hardware for this system, consisting of: a biplane x-ray image-intensifier video system plus a video quantizer and flying-spot scanner assembly for electronic recognition and measurement of the diameters of the opacified left ventricular chamber at each of the 60-80 horizontal lines contained in the 60-per-second biplane video images of this chamber, has been described fully in the 1968-1970 reports. This complete system is now operational. The techniques for the very high speed on-line transfer of data (64,000 samples/second) from this system to the CDC 1700-3300 computer facility and the processing of these data, which are described in the October 1969 progress report, are progressively improved and extended. The analysis of the accuracy and reproducibility of the 60/second values of the shape and volume of the left ventricle, included in the 1970 reports, is being extended.

2. The weakest link in the system has been the video disc recorder required for stop-action replay of single video fields during operator interactive adjustment of video signal levels to facilitate electronic recognition of the borders of the biplane silhouettes on each of the 60-80 horizontal video lines which constitute the two images of the object (e.g., left ventricular chamber) under study.

   Data Memory, Incorporated have failed in their promise to deliver a video disc recorder with balanced outputs from the two heads, and as of March 1970 have admitted that the required $\pm 1\%$ amplitude, linearity, and phase lag matching between the two channels can not be achieved with their current recorder.

   Consequently, a Model DR-10 video disc recorder, a prototype machine of which was tested in our laboratory during a 10-day period in May, 1970 and fulfilled these operational requirements, was ordered from Ampex Corporation. The final machine was received in the laboratory on August 25, 1970 and highly successful experiments comparing stroke volume values determined by dye-dilution curves and roentgen videometry have been carried out.

3. More detailed studies will now be carried out concerning the accuracy of measurements of the stroke volume and rate of change of volume of the left ventricle by this system in dogs studied without thoracotomy

by comparison of videometric values with simultaneous measurements by the accepted and independent methods of dye-dilution determinations of cardiac output and beat-to-beat recording of stroke volume from electromagnetic flowmeters implanted on the ascending aorta.

4. When miniature implantable transducers for measurement of the internal dimensions of the left ventricle are made available by Dr. Harold Sandler of NASA, Ames Research Center, studies of the feasibility of calibrating these transducers for dynamic measurements of ventricular volume on the basis of simultaneous determinations using biplane roentgen videometry will be instituted.

   It is envisaged that these developments will lead to feasible techniques for remote monitoring of changes in ventricular volume of large nonhuman primates during space flight, particularly the zero gravity state.

B. Development of telemetry techniques for study of cardiorespiratory effects of changes in the gravitational-inertial force environment in chimpanzees:

   1. In spite of the initial discouraging results, studies in dogs are being continued with the active participation of Dr. Harold Sandler and Mr. Sol Rositano of NASA, Ames Research Center, of the feasibility and accuracy of phasic blood flow measurements of regional pulmonary blood flow, using telemetered signals from ultrasonic cuff transducers implanted on the main, right, and left pulmonary arteries. The relationship of the effects of plus and minus G_y (lateral) acceleration on telemetered blood flow values through the right and left pulmonary arteries to the simultaneous regional distribution of isotopically tagged microsphere emboli in the two lungs during these changes in the force environment will be of particular interest.

   2. If these preliminary studies are successful, Dr. Sandler will supply and assist in the implantation of a multichannel telemetry-transducer system into one of the five chimpanzees available for study in our laboratory. This system will then be used for study of the cardiovascular reactions of the chimpanzee in the unanesthetized state and during exposure to acceleration.

C. Investigation of effects of changes in the gravitational-inertial force environment on intrathoracic pressure relationships and consequent alterations in the spatial distribution of pulmonary blood flow, ventilation, and arterial-venous shunts in the lungs of dogs and chimpanzees studied without thoracotomy:

   1. The operator interactive computer controlled technique, described in the October 1969 progress report, for determination and display of the spatial distribution of differentially isotope tagged 35μ microspheres (blood flow) within simulated three-dimensional displays of the anatomic outline of the lungs and their component lobes will continue to be used to study alterations in the distribution of pulmonary blood flow with changes in body position and during acceleration. Particular attention is being devoted to the

vertical redistribution of blood flow against a hydrostatic pressure gradient which is believed to be responsible for the decrease in pulmonary arterial-venous shunt which has been observed to occur in a few dogs and more frequently in chimpanzees towards the end of exposures of one or more minutes in duration to accelerations of 5-7G.

2. Development and application of the isotope tagged aerosol technique, described in the October 1969 report, for study of regional pulmonary ventilation will be continued.

3. A study of the changes in spatial configuration of the tracheal-bronchial tree and the pulmonary parenchyma in different body positions and during acceleration has been initiated, using inhaled tantalum dust for roentgenographic visualization of the pulmonary airways and one millimeter diameter lead beads impacted in peripheral vessels to tag multiple sites in the pulmonary parenchyma. These changes, measured from biplane roentgengograms of the thorax and 60-per-second video roentgenograms recorded on videotape, will be correlated with simultaneous measurements of the spatial distribution of pulmonary blood flow, ventilation, and arterial-venous shunts.

4. Studies described in the April 1970 report using constant volume liquid immersion body support and restraint system and its incorporated intermittent whole body negative and positive pressure respiratory assembly, developed in this laboratory, will be continued to determine the effects of this type of whole body restraint on intrathoracic pressure relationships and regional blood flow, ventilation,aand arterial-venous shunts in the lungs of dogs studied at 1G and during acceleration when: (1) breathing air or 99.6% oxygen at controlled residual and tidal volumes, and (2) fluid breathing under similar circumstances using the liquid fluorocarbon FC 80 and an associated oxygenator pump assembly, as described in the October 1969 and 1970 reports.

   Studies with fluid breathing in eight dogs with this assembly have demonstrated the feasibility of this technique. The assembly is being modified to provide more accurate monitoring and control of residual volume of fluorocarbon in the lung so that accurate continuously variable control of the functional residual volume, total volume, and respiratory rate of the fluorocarbon can be achieved.

   A cooperative study is being initiated with the 3M Company to develop a technique for tagging fluorocarbon liquid by inclusion of an isotopic atom in the fluorocarbon molecule or use of a fluorocarbon soluble-water insoluble dye. If a suitable tagging technique can be developed, more accurate determinations of the functional residual volume of the lungs will be possible during fluorocarbon breathing and the mixing characterisitics of the tidal volume with the total volume of fluorocarbon in the lungs can be studied.

The use of flow-through PO2, PCO2, and pH electrode assemblies for continuous recording of these variables in, and volume of inspired and expired fluorocarbon during centrifugation is being investigated in cooperation with the Beckman Instrument Company. If suitable techniques for these measurements can be evolved, studies of the rate of oxygen utilization, respiratory quotient, and alveolar - blood PO_2 and PCO_2 gradients will be possible during fluid breathing at 1G and during exposures to acceleration.

The results obtained during the 1970 grant period demonstrate conclusively that the dependent pulmonary arterial-venous shunting and displacement of the heart, which are unavoidable consequences of sustained exposures to high acceleration when breathing air or oxygen, can be prevented by liquid breathing.

If a practical technique can be developed for air-breathing animals, including man, to maintain normal blood gas tensions while respiring a liquid with a specific gravity equivalent to that of blood and tissue without serious sequelae, it would be possible to withstand extremely high transient or sustained accelerations and environmental pressures without injury of the lungs. Presumably, also the incompressible nature of the liquid state would make it possible to withstand the tremendous pressures encountered at deep regions of the ocean floor and with concomitant avoidance of the risk of decompression. Extravehicular survival by the use of liquid breathing in the extreme depths of the ocean may also be feasible.

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October 15, 1970

EHW:JF

PUBLICATIONS

1. Ritman, E. L., R. E. Sturm, and E. H. Wood: Comparison of volume of canine left ventricular casts and angiograms using biplane and monoplane roentgen videometry.
The Physiologist 13:294 (August) 1970.

2. Ritman, E. L., R. E. Sturm, and E. H. Wood: A biplane roentgen videometric technique for dynamic studies of shape and volume of the left ventricle. Federation Proceedings 29:719 (March-April) 1970.

3. Sass, D. J., E. L. Ritman, P. E. Caskey, N. Banchero, and E. H. Wood: Modification of the cardiopulmonary effects of acceleration by water immersion and liquid breathing.
The Physiologist 13:301 (August) 1970.

4. Greenleaf, J. F., E. L. Ritman, D. J. Sass, and E. H. Wood: Changes in distribution of pulmonary blood flow during acceleration.
The Physiologist 13:212 (August) 1970.

5. Sass, D. J., E. L. Ritman, P. Caskey, J. Greenleaf, N. Banchero, D. Mair, and E. H. Wood:
Effects of $+G_y$ acceleration on blood oxygen saturation and pleural pressure relationships in dogs breathing first air, then liquid fluorocarbon in a whole body water immersion respirator.
Proceedings of 27th meeting of the Aerospace Medical Panel of AGARD NATO, September 15-17, 1970, Garmisch-Partenkirchen, Germany (in press).

6. Katori, R., D. DeS Amorim, R. A. Theye, and E. H. Wood:
Influence of body position on regional pulmonary arterial-venous shunts in intact dogs.
Journal of Applied Physiology 29:288-296 (September) 1970.

7. Avasthey, P., C. M. Coulam, and E. H. Wood:
Position-dependent regional differences in pericardial pressures.
Journal of Applied Physiology 28:622-629 (May) 1970.

8. Coulam, C. M., W. H. Dunnette, and E. H. Wood:
A computer-controlled scintiscanning system and associated computer graphic techniques for study of regional distribution of blood flow.
Computers and Biomedical Research 3:249-273 (June) 1970.

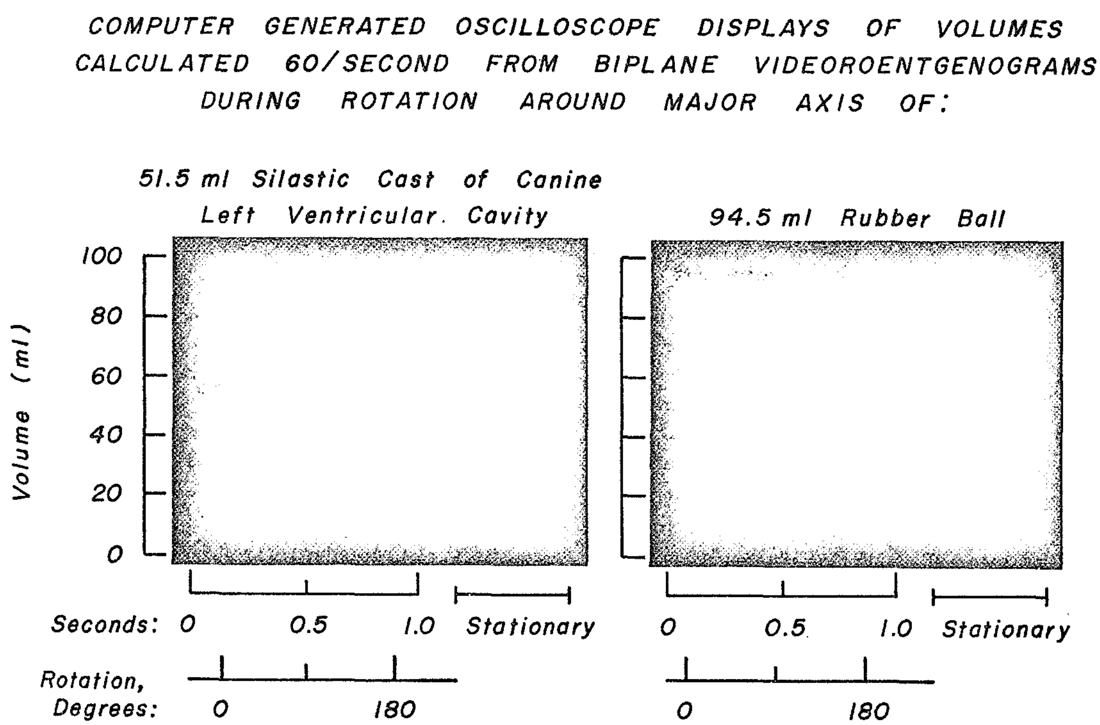


Figure 1 Computer generated oscilloscope displays of individual sixty-per-second values from volume of cast of left ventricle (left panel) and a rubber ball (right panel) during rotation around a major axis orthogonal to the plane of intersection of the orthogonal roentgen beams (left portion of each panel) and when maintained stationary at this point (right portion of each panel). The computed values for ventricular volume were calculated by assuming that each of the 70 cross sections of the ventricular chamber which constituted the two video images were elliptical in shape. The amplitude of the sinusoidal variation in the calculated values of the volume of the cast, which would be expected to result during each 90° of rotation of an object with an approximately elliptical cross section, is about 7% of the mean value.

The small inherent variability of the roentgen video measurement system proper can be judged during the period when the cast was stationary (left panel) and during the entire period of measurement of the volume of the ball (right panel).

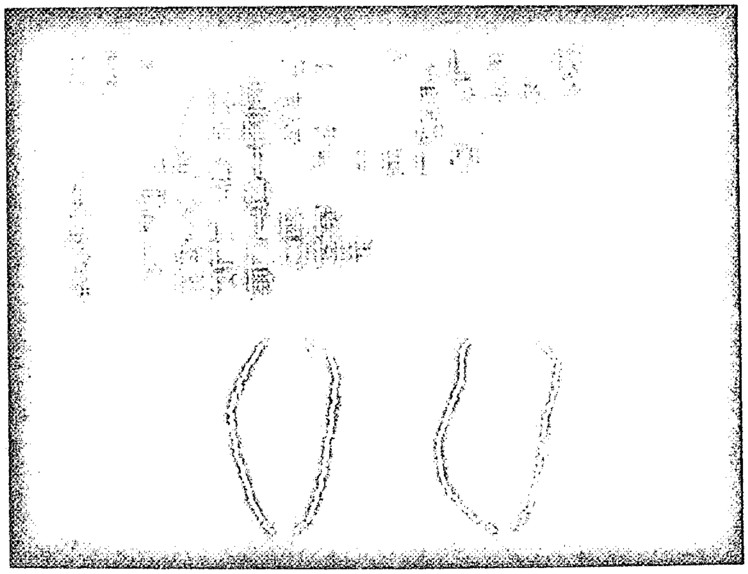


Figure 2 Picture of the face of storage oscilloscope at peripheral computer station juxtaposed to assembly for biplane roentgen videometry showing computer generated display of data from a single video field plus the options contained in the computer program and on call via the remote station keyboard by the operator carrying out the data analysis procedure.

The computer reconstruction of the biplane silhouettes of the ventricle based on the count values generated by the border recognition digital clock assembly is displayed on the bottom half of the storage tube raster. Definitions of the computer generated symbols or statements above these silhouettes are as follows:

II: The number of video lines between the cephalad and caudad borders of the ventricle.

Volume: The calculated volume in mm^3 of the ventricle for this video field; in this instance the number of the video field was 0.

LV Pres: Pressure in the ventricle recorded simultaneously with this video field (in this instance, 0) since this is a display of the silhouettes of the silastic rubber cast of the left ventricular cavity of a dog, data from which are shown in Figure 1.

0-4: Indicate the number of the key on the keyboard of the peripheral computer station which the operator can depress to order the computer to proceed to the next step in the analysis procedure he wishes the computer to carry out, as follows:

Figure 2 (continued)

0: Proceed to analysis of next video field.

1: Analyze a specified number of the next video fields. The number of fields the operator wishes to have analyzed is specified in the next order to the computer.

2. Filter the border recognition data to reduce irregularities.

3. Generate a Calcomp plot of this field.

4. Compare the borders of this field with that of the prior field as a basis for estimating errors in border recognition.

COMPUTER GENERATED DISPLAY OF BALLOON VOLUMES
COMPUTED FROM BIPLANE ROENTGEN VIDEOGRAM
RECORDED DURING INJECTION OF 9.8 ml 69% RENOVIST
(Initial Volume: 32.1 ml)

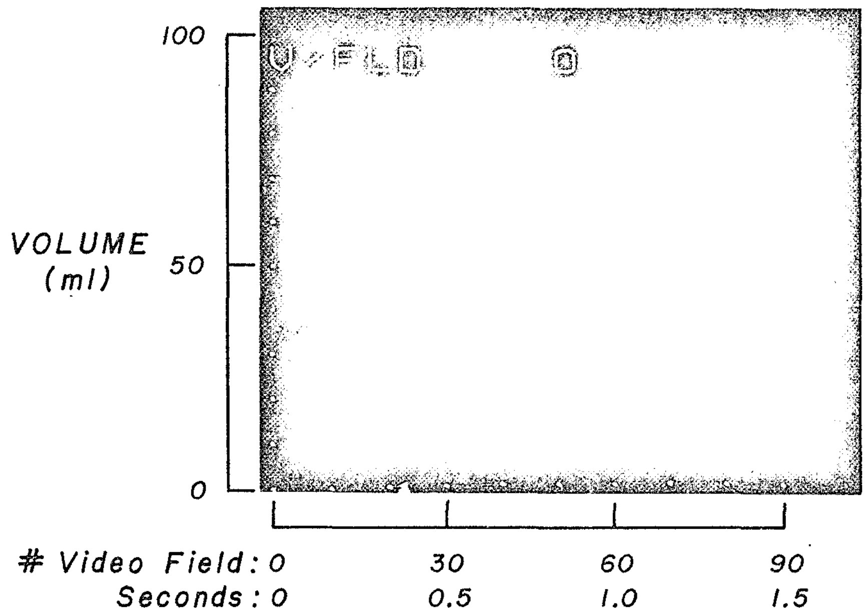


Figure 3 Volume values calculated from 100 successive video fields of a videotape recording of a biplane roentgenogram of a balloon during injection of 69% renovist which increased its volume from 32.1 to 41.9 ml in a period of 0.4 seconds.

ASSEMBLY FOR BIPLANE VIDEOROENTGENOGRAPHY

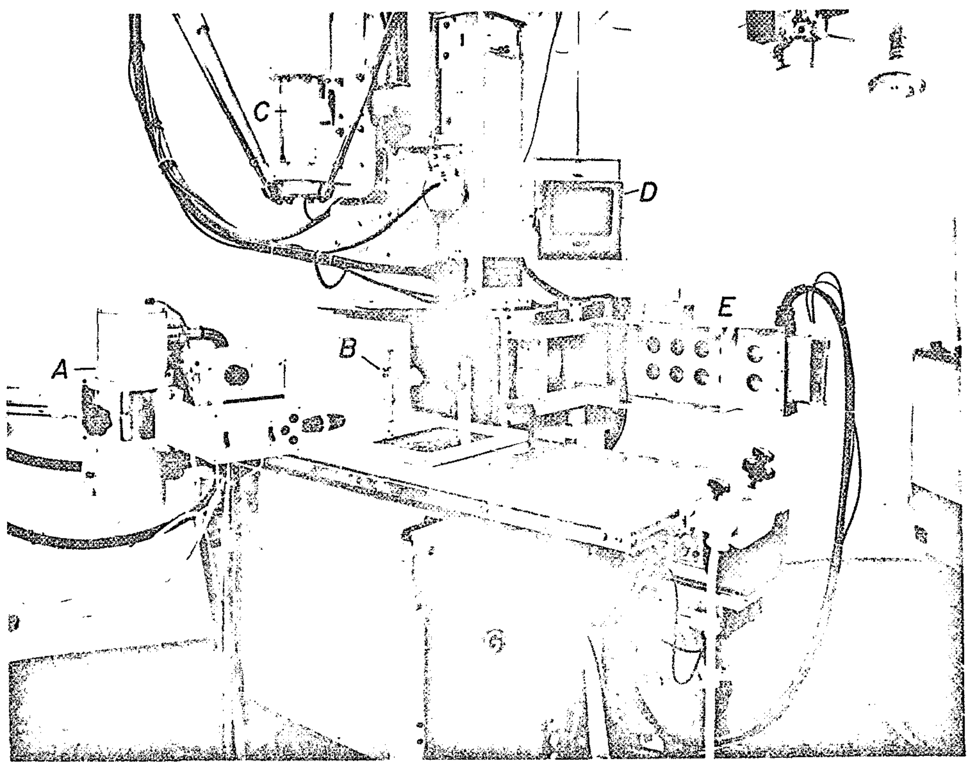


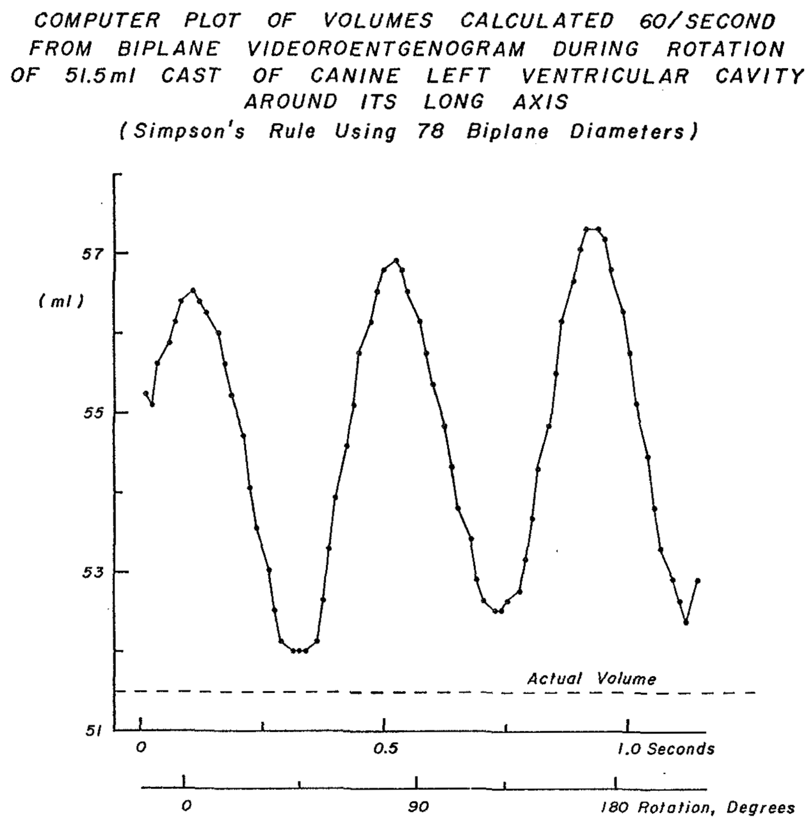
Figure 4 Assembly for biplane videoroentgenography set-up for measurement of volume of silastic cast of canine left ventricle during rotation of the cast on a steel rod (B) transecting its long axis.

(A) x-ray tube for horizontal image intensifier-image orthicon video camera assembly (E).

(C) vertical image intensifier-image orthicon video camera assembly, the x-ray source for which is enclosed in the support (G) of the fluoroscopic table.

(D) television monitor for viewing the biplane images from the horizontal and vertical camera assemblies simultaneously in the same video field.

(F) control console for x-ray tubes.



<u>Figure 5</u> An expanded computer generated plot of the data shown in the left panel of Figure 1 during rotation of the cast through an angle of about 200°. Note that the true volume of the cast, marked by the dashed line, was 51.5 ml. In addition to the 90° periodicity in the values of the calculated volume, there is a much smaller amplitude 360° periodicity in the volume values due to the fact that the cross sections are not elliptical in shape and because the angular relationship of the actual major and minor diameters of each cross section to the two diameters measured from the 78 video lines making up the video image varies continuously during rotation and to different degrees along the long axis of the cavity.

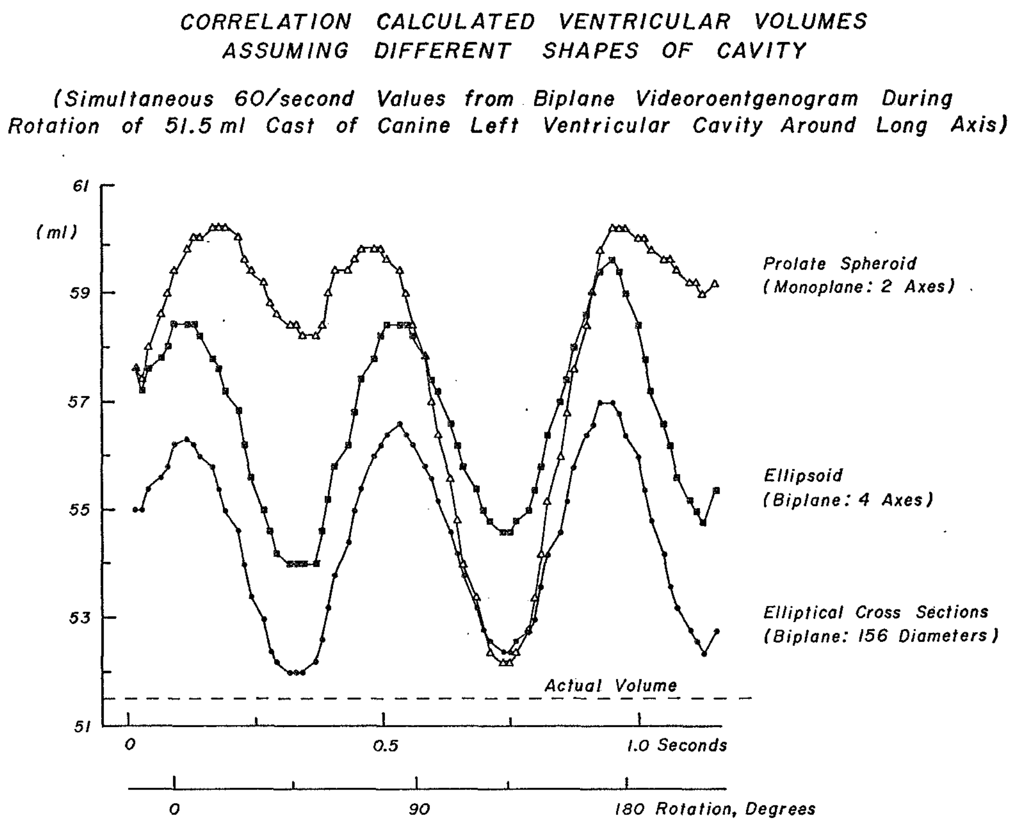


Figure 6 Computer generated plot of simultaneous 60-per-second values for the volume of a cast of canine left ventricular cavity calculated assuming different shapes of the cavity. The diameters of the cast used for these calculations were measured by biplane roentgen videometry from a video roentgenogram recorded on magnetic tape during rotation of the cast around its long axis.

Note that calculated values overestimate the actual volume of the 51.5 ml cast by 0.5 to 9.0 ml, depending on the angular aspect at which the cast was viewed by the orthogonally oriented roentgen video assemblies shown in Figure 4. The volume values calculated assuming that the 78 measured cross sections of the cavity were elliptical in shape are identical to the values shown in Figure 5.

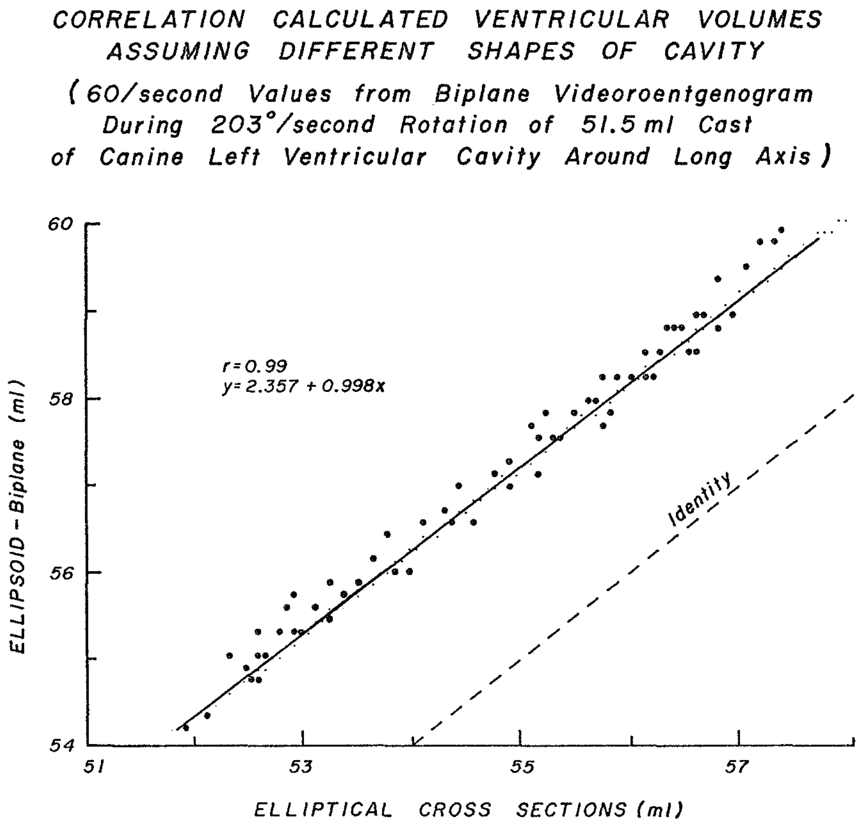


Figure 7 Computer generated plot showing correlation between values for the volume of cast of the cavity of a canine left ventricle calculated from simultaneous biplane roentgen videometric measurements, assuming: (1) that the cavity was an ellipsoid and using the three orthogonally oriented major diameters, and (2) that each of the 78 cross sections, the orthogonal diameters of which were measured by videometry, were elliptical in shape.

The biplane videometric diameter measurements were made from each biplane video field recorded 60 times per second during rotation of the cast through an angle of about 200° around its long axis during a period of one second.

Y is the linear regression equation between the two sets of values indicated by the solid line, and r the correlation coefficient of 0.99. Identical determinations by the two methods would fall on the dashed line.

Figure 7 (continued)

Note that, although there is an excellent correlation between the two sets of values, both methods resulted in an overestimate of the volume of the 51.5 ml cast, which ranged from 0.5 to 6.0 ml for the elliptical cross section and from 3.0 to 8.5 ml for the ellipsoid shape assumptions, respectively.

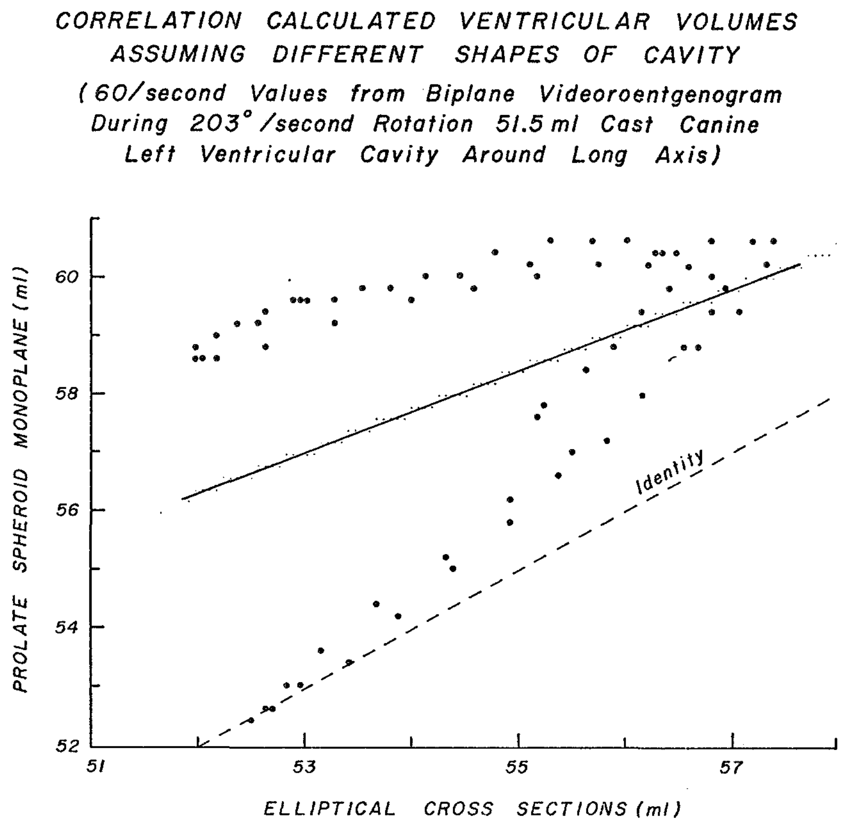


Figure 8 Computer generated plot showing correlation between values for the volume of cast of the cavity of a canine left ventricle calculated from simultaneous roentgen videometric measurements, assuming: (1) that the cavity was a prolate spheroid and using the orthogonally oriented diameters measured from the monoplane projections recorded by the vertically oriented roentgen-video assembly (Figure 4), and (2) that each of the 78 cross sections, the orthogonal diameters of which were measured from the biplane projections recorded simultaneously by the vertical and horizontal roentgen-video assemblies, was elliptical in shape. See legend for Figure 7 for additional details.

Note that the overestimates of from 1 to 10 ml of the values obtained from a single projection, and assuming the shape of the 51.5 ml ventricular cavity was a prolate spheroid, were generally larger than simultaneous values obtained by assuming the multiple cross sections were elliptical in shape.

COMPUTER PLOTS OF SIMULTANEOUS LEFT VENTRICULAR PRESSURES AND VOLUMES CALCULATED 60/SECOND FROM BIPLANE VIDEOANGIOGRAM USING SIMPSON'S RULE WITH 60-70 BIPLANE DIAMETERS

(Dog 10.5kg, Morphine - Pentobarbital Anesthesia, 8 ml 69% Renovist into Left Ventricle)

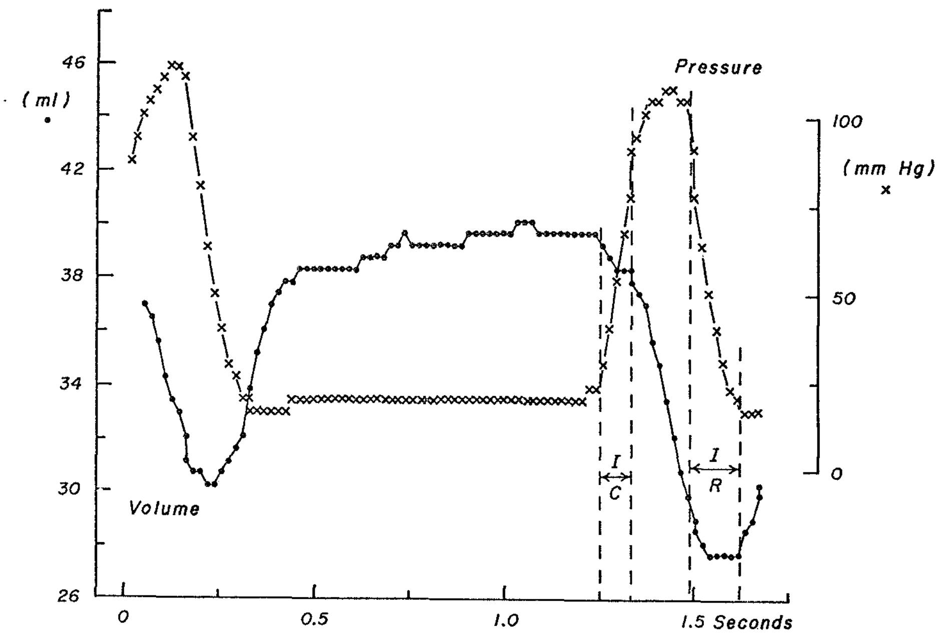


Figure 9 Computer generated plot of left ventricular volume and pressure recorded from a dog with cardiac decompensation caused by a slow idioventricular rhythm following chronic percutaneously produced heart block. The values for ventricular volume were calculated 60 times per second from an angiogram recorded on videotape during the first cardiac cycle following completion of the injection of 8 ml 69% renovist into the left ventricle assuming that each of the 60-70 cross sections, the orthogonal diameters of which were measured by roentgen videometry, was elliptical in shape. Intraventricular pressure was recorded simultaneously on the same videotape. The double-ended horizontal arrows, labeled IC and IR, indicate the isovolumic contraction and relaxation phases of the ventricle, respectively. The small, less than 0.5 ml, changes in calculated volume values during these phases of the cycle are presumably artifactual and caused by the changes in angular position and shape of the ventricular cavity which, because of the elliptical cross section assumption, would be expected to result in a change in the calculated values for the volume of this cavity, as illustrated in Figure 5.

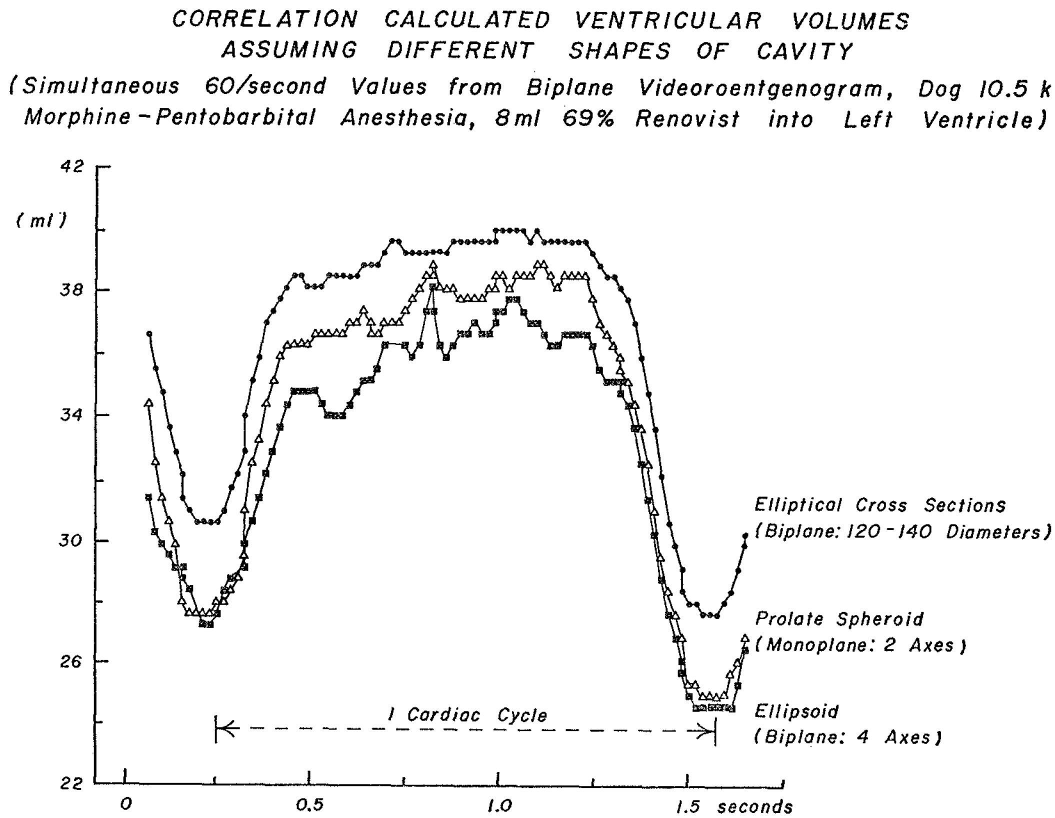
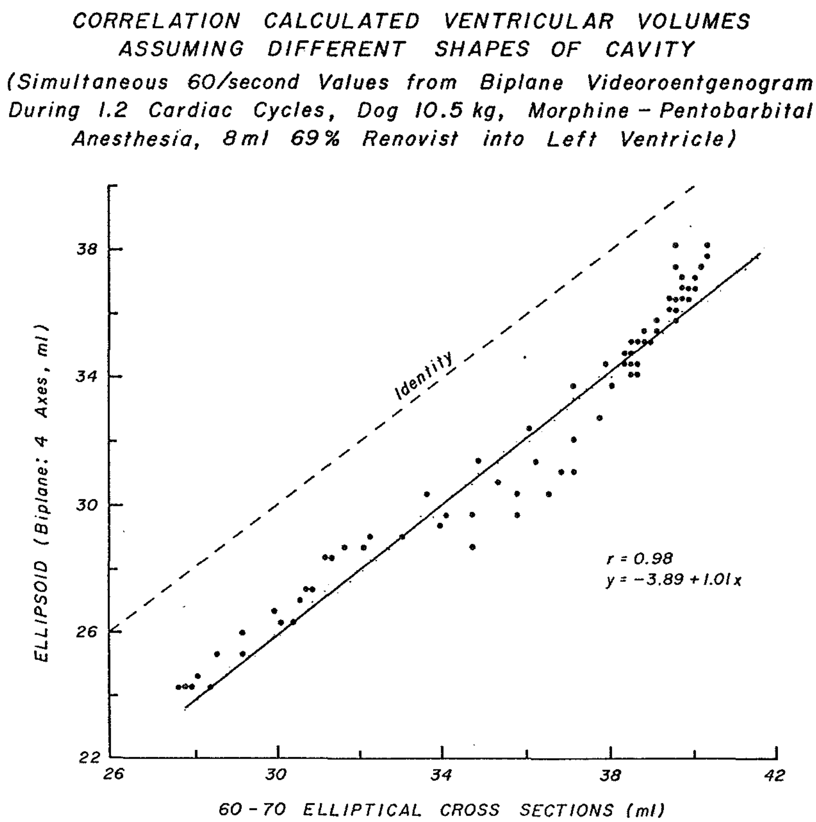


Figure 10 Computer generated plot of simultaneous values for the volume of the left ventricle calculated 60 times per second assuming three different shapes of the ventricular cavity during the same cardiac cycle, as shown in Figure 9. See legends for Figures 6 and 9 for additional details.

Note the relatively constant differences in the three sets of volumes obtained by the three methods, and that the total changes in volume during this heart beat (i.e., the stroke volumes) determined by each method were similar.



<u>Figure 11</u> Computer generated plot showing correlation between values for left ventricular volume of a dog calculated from simultaneous biplane roentgen videometric measurements, assuming: (1) that the cavity was an ellipsoid and using the three orthogonally oriented major diameters, and (2) that each of the 60-70 cross sections, the orthogonal diameters of which were measured by videometry, were elliptical in shape.

The biplane videometric diameter measurements were made from each video field recorded 60 times per second during the cardiac cycle shown in Figure 9. See legend for Figure 9 for additional details.

Y is the regression equation between the two sets of values indicated by the solid line, and r the correlation coefficient of 0.98. Identical determinations by the two methods would fall on the dashed line. Note that, although there is an excellent correlation between the two sets, the values obtained by the elliptical cross section assumption averaged about 4 and ranged from 1 to 6 ml smaller than the simultaneous values obtained by assuming an ellipsoid shape of the cavity.

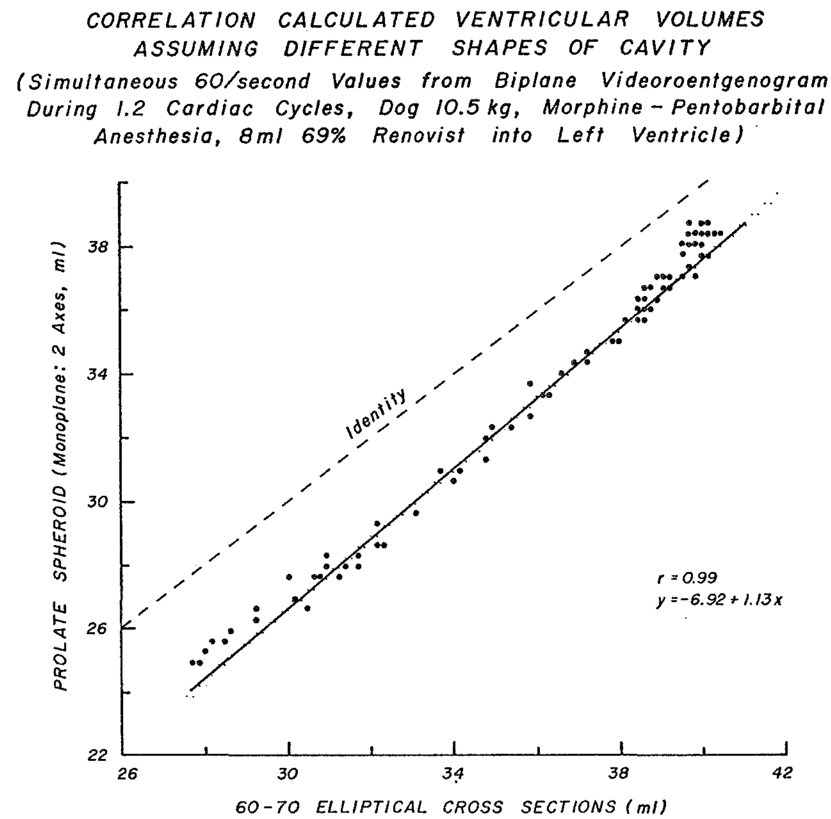


Figure 12 Computer generated plot showing correlation between values for left ventricular volume of a dog calculated from simultaneous roentgen videometric measurements, assuming that: (1) the cavity was a prolate spheroid and using the orthogonally oriented diameters measured from the left anterior oblique projection, and (2) each of the 60-70 cross sections, the orthogonal diameters of which were measured from the left anterior and posterior oblique projections, was elliptical in shape. See legend for Figure 11 for additional details.

Note that although there is an excellent correlation between the two sets, the values obtained by the elliptical cross section assumption averaged about 3, and ranged from 0.5 to 4.0 ml smaller than the simultaneous values obtained by the monoplane method.

The slope of the regression line of 1.13 suggests that stroke volume values obtained by the monoplane method will average about 13% larger than simultaneous values obtained by the biplane methods.

Figure 13

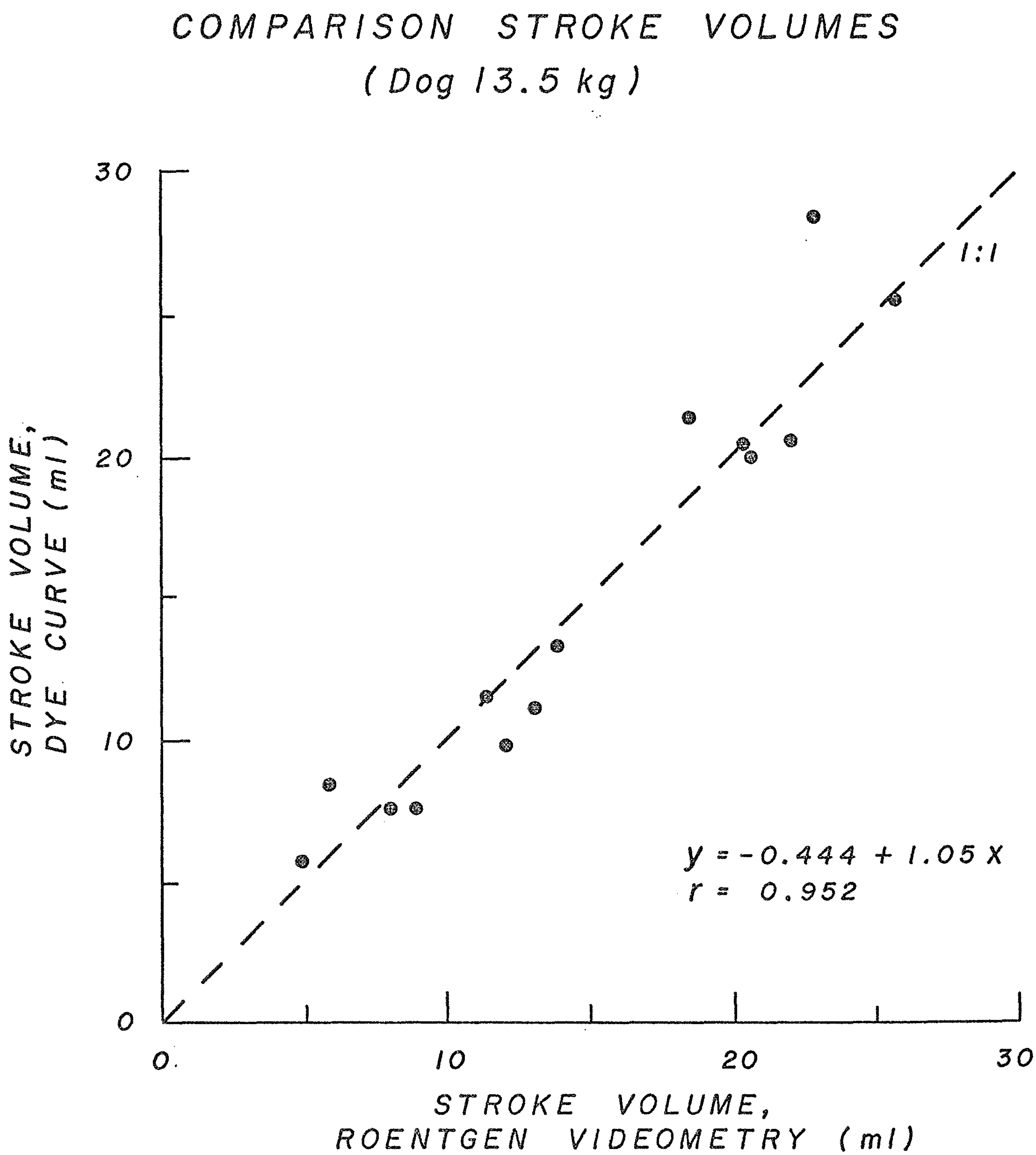

COMPARISON STROKE VOLUMES
(Dog 13.5 kg)
STROKE VOLUME,
DYE CURVE (ml)
0
10
20
30
0.
10
20
30
STROKE VOLUME,
ROENTGEN VIDEOMETRY (ml)
1:1
y = -0.444 + 1.05 X
r = 0.952

Figure 13 Comparison of values for stroke volume determined in close temporal proximity by arterial dilution curves of indocyanine green and by biplane roentgen videometry in a dog anesthetized with morphine and sodium pentobarbital and studied without thoracotomy. Complete atrial-ventricular dissociation (heart block) had been produced by a percutaneous technique and an electromagnetic flowmeter implanted on the ascending aorta approximately six weeks prior to these studies. Determinations were made at heart rates ranging from 45 to 180 beats per minute induced by a coupled atrial and ventricular pacemaker attached to bipolar electrode catheters inserted via the left external jugular vein and their tips positioned near the atrial-superior caval juncture and the right ventricular outflow tract, respectively.

Replicate curves were recorded from the femoral artery at each heart rate and cardiac output and central blood volume calculated on-line by a CDC 3300 digital computer following injections of indocyanine green into the right atrium. Biplane videocardiograms were recorded on videotape shortly after each set of dilution curves by injecting 8 ml 69% renovist into the left ventricle via a catheter inserted transseptally from the right external jugular vein. The stroke volume values determined by dye dilution are average values for the cardiac cycles which occurred during the period from injection of the dye to the peak deflection of the curve while the videometric values are measurements from individual cardiac cycles (i.e., the first heart beat following completion of each injection of contrast medium).

Y is the regression equation and r the correlation coefficient of 0.95 between the two sets of values. Identical values by the two methods would fall on the dashed line.

Figure 14

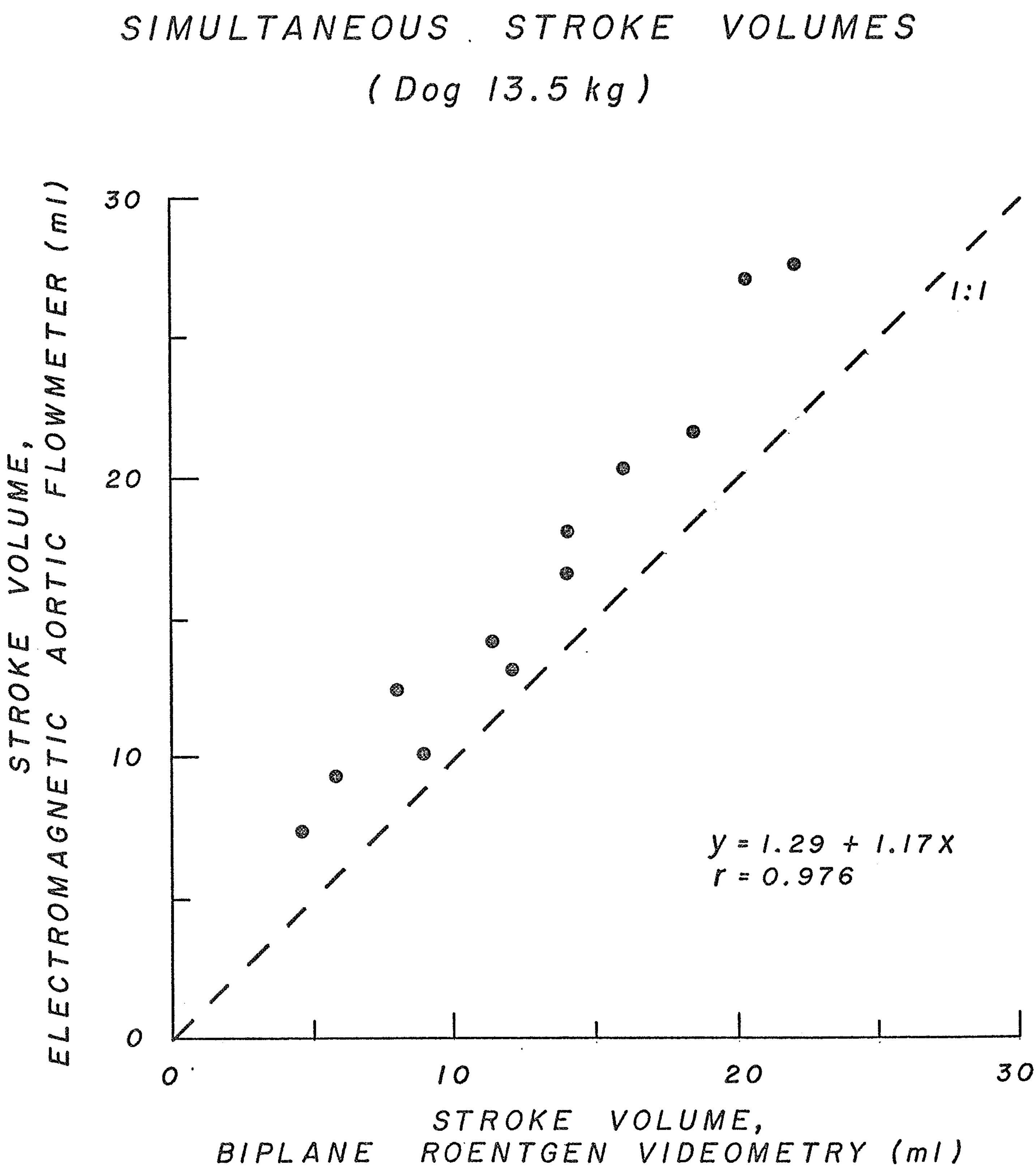

SIMULTANEOUS STROKE VOLUMES
(Dog 13.5 kg)
STROKE VOLUME,
ELECTROMAGNETIC AORTIC FLOWMETER (ml)
30
20
10
0
0
10
20
30
1:1
y = 1.29 + 1.17X
r = 0.976
STROKE VOLUME,
BIPLANE ROENTGEN VIDEOMETRY (ml)

Figure 14 Comparison of simultaneous stroke volume values determined by biplane roentgen videometry and by an electromagnetic flowmeter on the ascending aorta in a dog anesthetized with morphine and sodium pentobarbital and studied without thoracotomy. See legend of Figure 13 for additional details.

The aortic flowmeter was calibrated in vivo on the basis of determinations of cardiac output from dilution curves of indocyanine green and simultaneously recorded aortic flow pulses.

Y is the regression equation and r the correlation coefficient of 0.976 between the two sets of values. Identical values by the two methods would fall on the dashed line. Note that, although there is a close correlation between the stroke volumesfor the same heart beats determined by these two independent methods, the flowmeter values average approximately 17% larger than those determined by videometry.

Figure 15

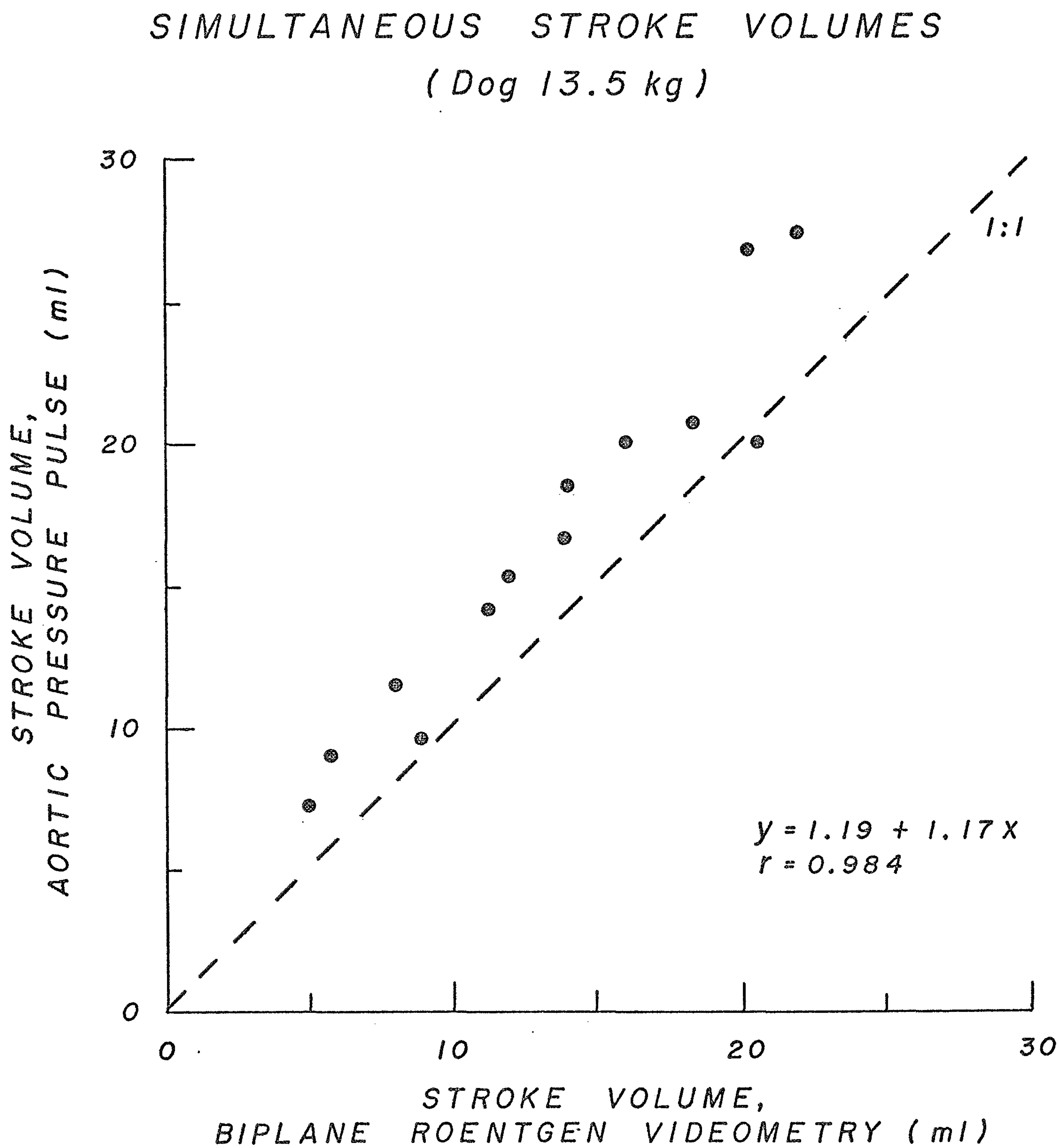

SIMULTANEOUS STROKE VOLUMES
(Dog 13.5 kg)
STROKE VOLUME,
AORTIC PRESSURE PULSE (ml)
STROKE VOLUME,
BIPLANE ROENTGEN VIDEOMETRY (ml)
0
10
20
30
1:1
y = 1.19 + 1.17 X
r = 0.984

Figure 15 Comparison of simultaneous stroke volume values determined by biplane roentgen videometry and by a new computerized aortic pressure pulse method (Bourgeois, M. J. et al, unpublished data) in a dog anesthetized with morphine and sodium pentobarbital and studied without thoracotomy. See legend of Figure 13 for additional details.

The aortic pressure pulse method was calibrated on the basis of determinations of cardiac output from dilution curves of indocyanine green and simultaneously recorded pressure pulses.

Y is the regression equation and r the correlation coefficient of 0.98 between the two sets of values. Identical values by the two methods would fall on the dashed line. Note that, although there is a close correlation between the stroke volumes for the same heart beats determined by these two independent methods, the aortic pressure pulse values average about 17% larger than those determined by videometry.

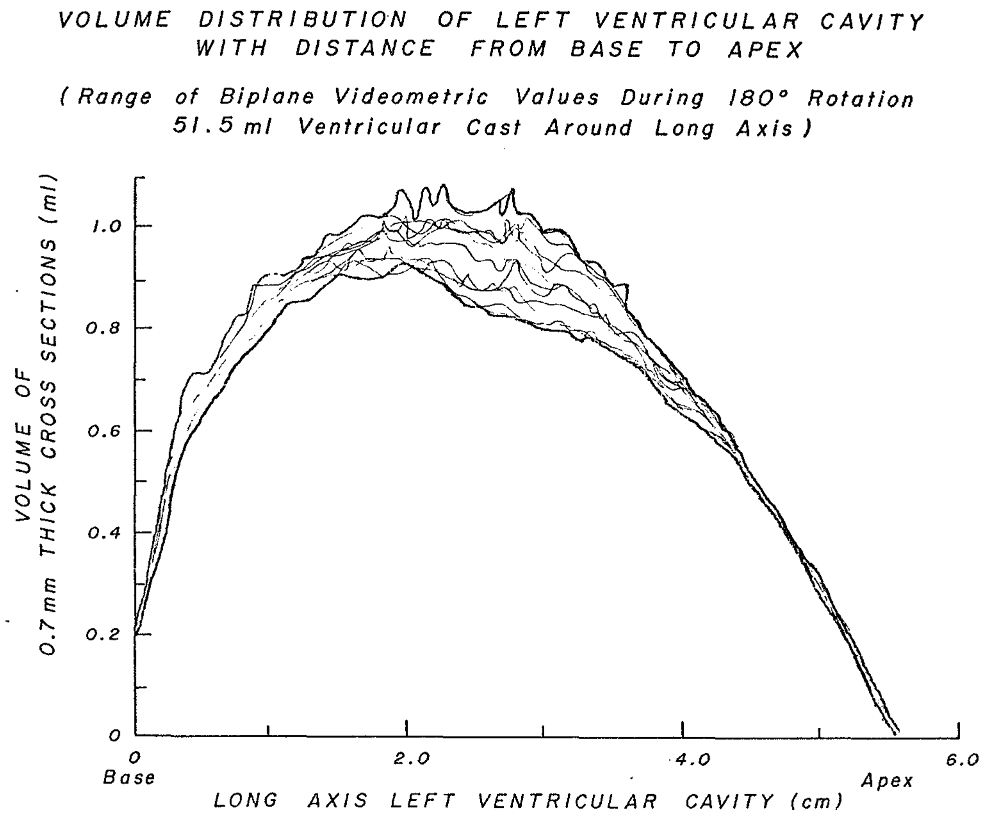


Figure 16 Variation in calculated volumes of cross sections of the left ventricular cavity in relation to the distance of each cross section from the basal border of the heart. The plot shows the range of values for the total set of seventy-seven 0.7 mm thick cross sections constituting the ventricular cavity, the orthogonal dimensions of which were determined 60 times per second by roentgen videometry while the cast of the cavity was rotated 180° about its long axis in about 0.9 seconds. Volume calculations for each cross section were based on the assumption that each was elliptical in shape. This silastic rubber cast was made from a dog's ventricle which was arrested and fixed during diastole.

Note that the smallest variation in calculated cross-sectional volumes with change in the angular aspect of the cast viewed by the biplane videometry system was obtained in the apical regions. This suggests that the shape of the cross sections in this region was nearly circular. The large variations in the mid-portion of the cavity are presumably caused by irregularities in shape of its cross sections due to protrusions of the papillary muscles into this region of the cavity.

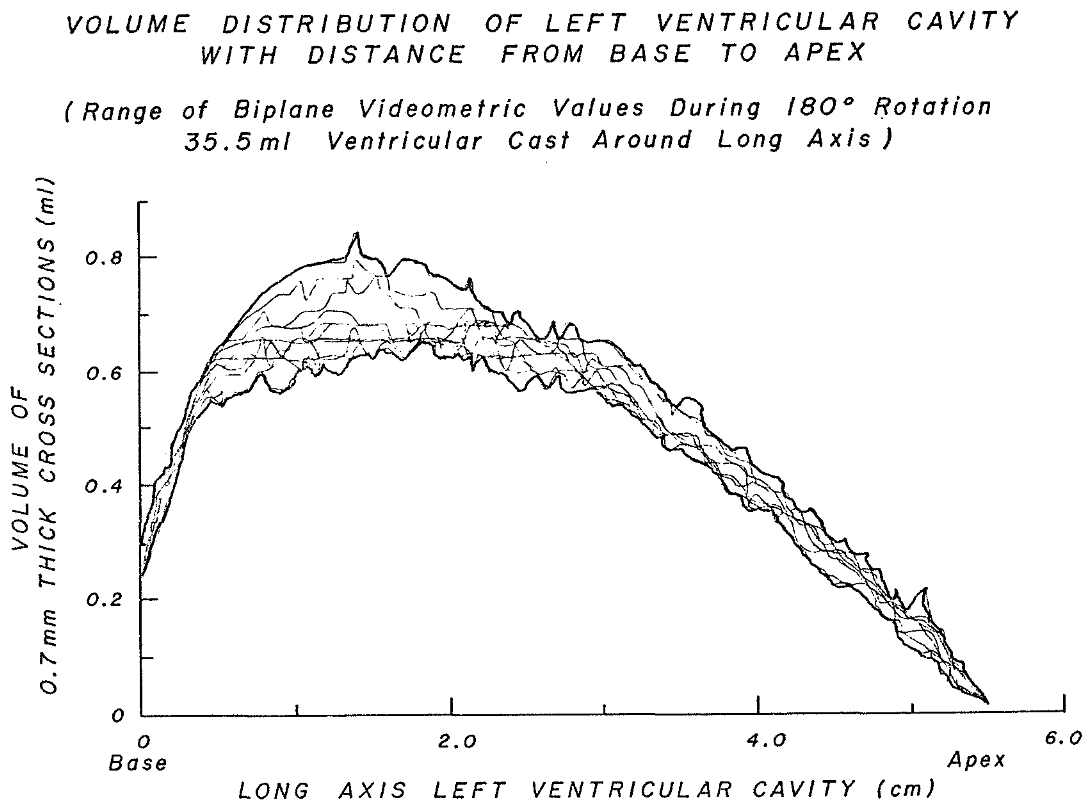


Figure 17 Variation in calculated volumes of cross sections of the left ventricular cavity in relation to the distance of each cross section from the basal border of the heart. This plot shows the range of values from the total set of seventy-five 0.7 mm thick cross sections constituting the ventricular cavity, the orthogonal dimensions of which were determined 60 times per second by roentgen videometry while the cast of the cavity was rotated 180° about its long axis in about 0.9 seconds. Volume calculations for each cross section were based on the assumption that each was elliptical in shape. This silastic rubber cast was made from a dog's ventricle which was arrested and fixed during systole.

Note the greater relative variation in cross-sectional volumes with change in the angular aspect viewed by the biplane system of this ventricular systolic cast than that found for the diastolic cast shown in Figure 16. This is presumably due to the increased variability of the shapes of cross sections of the ventricular cavity which pertains during systole.